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EXAMINER	
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ART UNIT	PAPER NUMBER
1649	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/577,658	CHABRIERE ET AL.	
	Examiner	Art Unit	
	Olga N. Chernyshev	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 September 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-32* is/are pending in the application.

4a) Of the above claim(s) *27 and 28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-21,23-26 and 29-32* is/are rejected.

7)☒ Claim(s) *22* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *01 May 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/1/6*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I in the reply filed on September 19, 2008 is acknowledged.

2. Claims 27 and 28 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on September 19, 2008.

3. Claims 16-26 and 29-32 are under examination in the instant office action.

Oath/Declaration

4. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:
Non-initialed and/or non-dated alterations have been made to the oath or declaration. See 37 CFR 1.52(c).

Claim Objections

5. Claims 18-21 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Claims 18-21 depend from claim 16, which is limited to a protein, while claims 18-21 encompass nucleic acids. Therefore, claims 18-21 can be infringed by a nucleic acid, which does not infringe claim 16. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in

proper dependent form, or rewrite the claim(s) in independent form. Applicant should note the "Infringement Test" for dependent claims in MPEP § 608.01(n). The test for a proper dependent claim is whether the dependent claim includes every limitation of the parent claim. A proper dependent claim shall not conceivably be infringed by anything, which would not also infringe the basic claim. In the instant case, the nucleic acid claims could be infringed without infringing the claims from which it depends, i.e. the protein claims. Therefore, they are improperly dependent and should be rewritten in independent form.

6. Claims 29-32 are objected to for being depended from a non-elected claim.

7. Claims 23 and 29-32 are objected to for recitation "sequence SEQ ID NO: 2" and "protein SEQ ID NO: 2", which are grammatically not correct. Amendment to recite "sequence of SEQ ID NO: 2" and "protein of SEQ ID NO: 2" would obviate this ground of objection.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

8. Claims 16, 17 and 18 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claims 16-18 fail to include any limitations which would distinguish the claimed proteins and nucleic acids from those which occur in nature. In the absence of the hand of man, naturally occurring products are considered non-statutory subject matter. *Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). Specifically, claims 16-18, as written, do not sufficiently distinguish over proteins and polynucleotides that exist naturally because the claims do not

particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. The claims should be amended to indicate the hand of the inventor, e.g., by insertion of "Isolated" or "Purified" as taught by the specification. Applicant should point to the basis in the specification for any amendment to the claims. See MPEP 2105.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 16-22, 24-26 and 29-32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

11. Claims 16-21, 24-26 are vague and ambiguous for recitation of a "sequence" in the context of meaning a "product". Applicant is advised that term "sequence" is a characteristic of a product - the linear order of monomers - such as amino acids or nucleic acids, and not the product - polypeptide or polynucleotide - itself. Amendments in the format of "an isolated protein comprising the amino acid sequence of SEQ ID NO: 1", for example, would obviate this ground of rejection.

12. Further, limitations "in particular", "preferably", "chosen in particular" in claims 16, 17, 21, 24-26 render the claimed subject matter indefinite because they depend on subjective opinion of the person practicing the invention. See MPEP 2173.05(b), "[t]he phrase "aesthetically pleasing" was held indefinite because the meaning of a term cannot depend on the

unrestrained, subjective opinion of the person practicing the invention. *Datamize LLC v. Plumtree Software, Inc.*, 417 F.3d 1342, 1347-48, 75 USPQ2d 1801, 1807 (Fed. Cir. 2005)".

13. Claim 20 is indefinite for reciting limitation "the polypeptide encoded by a nucleotide sequence encoding a protein". Specifically "the polypeptide", which is defined by "a protein" appears to be encompassed by the same molecule. Alternatively, it is obvious that a host cell expresses a plurality of polypeptides, however, it is not clear what "polypeptides" and "proteins" are intended by the claim. Clarification is required.

14. Claims 24 and 25 are vague and indefinite in so far as they employ the term "paraoxonase protein" as a limitation. This term is appears to be novel, and without a reference to a precise amino acid sequence identified by a proper SEQ ID NO: one cannot determine the metes and bounds of "paraoxonase protein" or variants thereof. Moreover, because the instant specification does not identify that property or combination of properties which is unique to and, therefore, definitive of a "variant of the paraoxonase protein", an artisan cannot determine if a compound which meets all of the other limitations of a claim would then be included or excluded from the claimed subject matter by the presence of this limitation.

15. Regarding claim 25, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

16. Claim 26 is indefinite as being incomplete for omitting essential elements and steps, such omission amounting to gaps between the claim preamble, steps and elements. See MPEP § 2172.01. Specifically, the claim is directed to "an assay method of the protein" and the metes and bounds of the recitation cannot be determined. It appears that the claim is directed to a

method of determining concentration of the protein of SEQ ID NO: 2 or SEQ ID NO: 3 by practicing the standard immunoassay; however, the claim recites several antibodies that are not defined by consistent terminology, unknown substrates and steps of fixing peroxidase to the plate, which renders the claimed subject matter vague and ambiguous. Applicant is advised to rewrite the claim to better express the claimed method.

17. Claims 29-32 are vague and indefinite in so far as it employs the term "diseases linked to hyper- [or hypo-]phosphataemia" or "linked to the formation of atheroma plaques" as limitations. The instant specification does not provide a clear definition of these diseases and these terms are not specifically used in the art so that an artisan can readily determine if a particular disease or condition is linked or not linked to hyperphosphataemia or to the formation of atheroma plaques. Therefore, one skilled in the art would not know which pathological conditions are under diagnosis by practicing the steps of the methods in claims 29-32.

18. Claims 29-32 are further indefinite as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. Specifically, the claims fail to recite any active, positive and repeatable steps, reciting only the use of the assay method (which is not recited in claim 27 from which claims 29-32 depend from). Therefore, it is unclear what method/process applicant is intending to encompass.

19. Claim 22 is indefinite for being dependent from indefinite claims.

20. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

21. Claims 24, 25 and 29-32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

22. Claims 24 and 25 are directed to compositions intended for pharmaceutical/therapeutic use comprising proteins of SEQ ID NO: 1, 2 or 3 in combination with variants of paraoxonase proteins identified as proteins of SEQ ID NO: 4 to 11. It is noted that proteins of SEQ ID NO: 4-6 are human proteins, while proteins of SEQ ID NO: 7 to 11 are of different species. The instant specification fails to provide any evidence or sound scientific reasoning to support a conclusion that composition comprising proteins of different species, as currently recited, is suitable for administration and/or beneficial to treat any pathological condition. The art does not teach the use of this type of pharmaceutical compositions and the specification does not provide any guidance as how to use the claimed invention. Therefore, it would require undue experimentation on part of one of ordinary skill in the art to research and discover by himself how to practice Applicant's invention, as currently claimed.

23. Claims 29-32 are directed to methods for diagnosis of diseases linked to hyper- or hypophosphataemia or predisposition to such diseases by measuring the concentration of proteins of SEQ ID NO: 2 or 3 in a sample of blood obtained from an individual. The invention is based on disclosure of the structure of a novel human protein of SEQ ID NO: 1 (represented by proteins of SEQ ID NO: 2 and 3). The specification states that proteins of SEQ ID NO: 2 and 3 have structural similarity to the human phosphate-binding protein (p. 3 of the specification) and further that under experimental conditions, protein of SEQ ID NO: 2 bound radioactive

phosphate (p. 12). However, the instant specification is not found to be enabled for the method for diagnosis of any disease or condition by measuring concentration of proteins of SEQ ID NO: 2 or 3 because the specification does not provide any factual evidence or present a line of scientific reasoning as guidance for such method of diagnosis. There is no working examples, which would show that the claimed method was successfully practiced or reference to a similar method practiced in the prior art of record. Therefore, it would require undue experimentation for one skilled in the art to practice the instant claimed methods of diagnosis of diseases "linked to" hyper- or hypophosphataemia.

The factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and, (8) the breadth of the claims. *In re Wands*, 8 USPQ2d, 1400 (CAFC 1988).

As stated above, the instant specification discloses the structure of two novel phosphate-binding proteins, SEQ ID NO: 2 and 3 represented by common structure of SEQ ID NO: 1. Because these polypeptides are novel, the prior art of record is silent with respect to function or biological significance of these proteins. Generally, art recognizes the role of phosphate-binding proteins in the phosphate metabolism (see pp. 1-2 of the instant specification, for example). However, the particular role of these instant human phosphate-binding proteins of SEQ ID NO: 1, 2 or 3 is not disclosed. Furthermore, there is no evidence of record presented by the instant specification that any of these proteins are differentially expressed during any pathology,

including disease "linked to" hyper- or hypophosphataemia. While it is not necessary that Applicant understands or discloses the mechanism by which the invention functions, in this case, in the absence of such an understanding, no extrapolation can be made of the information regarding structural similarity of the novel disclosed polypeptide molecules to predicting their expression/secretion pattern during diseases related to disturbances in phosphate metabolism. Therefore, to use the novel claimed molecules in the diagnostic methods would require first to experiment and discover what is the biological role of these proteins in pathogenesis of the diseases "linked to" hyper- or hypophosphataemia", and then to assay for correlation of the concentration of the proteins in blood with the specificity or severity of the phosphate metabolism.

The standard of an enabling disclosure is not the ability to make and test if the invention worked but one of the ability to make and use with a reasonable expectation of success.

A patent is granted for a completed invention, not the general suggestion of an idea and how that idea might be developed into the claimed invention. If mere plausibility were the test for enablement under section 112, applicants could obtain patent rights to "inventions" consisting of little more than respectable guesses as to the likelihood of their success. In the decision of *Genentec, Inc, v. Novo Nordisk*, 42 USPQ 2d 100,(CAFC 1997), the court held that: "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable" and that "[t]ossing out the mere germ of an idea does not constitute enabling disclosure". The court further stated that "when there is no disclosure of any specific starting material or of any of the conditions under which a process is to be carried out, undue experimentation is required; there is a failure to meet the

enablement requirements that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art", "[i]t is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement".

The instant specification is not enabling because one cannot follow the guidance presented therein and practice the claimed methods without first making a substantial inventive contribution.

24. Claims 16-22 and 24-25 are further rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 16 and 17 are directed to polypeptides which are derivatives from the polypeptide of SEQ ID NO: 1 and encompass molecules with "substitution, suppression or addition of one or more amino acids" to the polypeptide of SEQ ID NO: 1; further, proteins that are homologous to the polypeptide of SEQ ID NO: 1 and any fragments of these derivatives and homologues. Claims 18-22 and 24-25 are dependent claims. In addition, claims 24-25 encompass variants of paraoxone proteins. The claims do not require that these polypeptides possess any particular conserved structure or other disclosed distinguishing feature; however, the claims explicitly require that the recited proteins "bind to phosphate". Thus, the claims are drawn to a genus of polypeptides that is defined only by sequence identity tied to the functional ability to bind phosphate. However, the instant specification fails to describe the entire genus of proteins, which are encompassed by these claims. In making a determination of whether the application

complies with the written description requirement of 35 U.S.C. 112, first paragraph, it is necessary to understand what Applicant has possession of and what Applicant is claiming. From the specification, it is clear that Applicant has possession of polypeptides which have the amino acid sequence of SEQ ID NO: 1, 2 and 3 and the corresponding polynucleotides. The claims, however, are drawn to derivatives, homologues and fragments of these defined proteins. Thus, the claims are not limited to a protein with a specific amino acid sequence. The claims only require the claimed polypeptides to share some degree of structural similarity to the isolated protein of SEQ ID NO: 1, 2 or 3 or even to polypeptides with no structural similarity to any of the disclosed polypeptides whatsoever (those fragments of the derivatives where any amino acid within the polypeptide of SEQ ID NO: 1 can be substituted, "suppressed" or added by one or more amino acid, see claim 16). The specification only describes proteins having the amino acid sequence of SEQ ID NO: 1, SEQ ID NO: 2 and SEQ ID NO: 3 and fails to teach or describe any other protein which lacks these amino acid sequences has the required phosphate binding activities possessed by the proteins of SEQ ID NO: 1, 2 or 3.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a reference to similarity to SEQ ID NO: 1. There is not even identification of any particular portion of the structure that must be conserved. As stated above, it is not even clear what region of the polypeptide of SEQ ID NO: 1 has the disclosed activity as the ability to bind phosphate.

Moreover, in case of fragments of derivatives with completely altered structure as in claim 16, the structure of the claimed molecules reads on any polypeptide in existence. The specification does not provide a complete structure of those polypeptides that are homologues and derivatives of the polypeptide of SEQ ID NO: 1 and fragments thereof that have the required activity and fails to provide a representative number of species for the claimed genus. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to

lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only isolated polypeptides comprising the amino acid sequence set forth in SEQ ID NO: 1 (or 2 or 3, which are variants of the polypeptide of SEQ ID NO: 1), but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Double Patenting

26. Applicant is advised that should claim 24 be found allowable, claim 25 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). In the instant case, because claim 25 fails to delineate the additional elements of the composition that provide for the recited intended use, the two claims encompass compositions comprising the same elements and therefore, are directed to the same subject matter.

Conclusion

27. Claim 22 is objected. Claims 16-21, 23-26 and 29-32 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Olga N. Chernyshev whose telephone number is (571) 272-0870. The examiner can normally be reached on 8:00 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey J. Stucker can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Olga N. Chernyshev, Ph.D.
November 21, 2008

/Olga N. Chernyshev/
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